



The Results of Uvulopalatopharyngoplasty in Patients with Moderate Obstructive Sleep Apnea Syndrome Having Cardiac Arrhythmias

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Abstract

Objectives: The goal of this practice was to explore whether the changes in arrhythmias after uvulopalatopharyngoplasty (UPPP) in patients with moderate obstructive sleep apnea syndrome (OSAS) who continued cardiac arrhythmias despite the use of antiarrhythmic drugs and those who could not tolerate the continuous positive airway pressure (CPAP) device. In addition, we evaluated the correlation between arrhythmias before and after UPPP.

Methods: This retrospective study included patients who have OSAS and cardiac arrhythmias, between 2008 - 2017 by the cardiology clinic and consulted by the ear, nose, and throat (ENT) clinic. Thirty eight patients were selected and underwent UPPP operation. The rhythm Holter follow-ups of the patients in the 1st month before UPPP (pre-UPPP) and after UPPP (post-UPPP) 6th month were performed. The recordings were transferred to the computer and evaluated with the Holter program, then visually examined and the parasitic regions were excluded. Sinus bradycardia (SB), atrioventricular block (AVB), atrial premature beat (APB), supraventricular tachycardia (SVT), and ventricular extrasystole (VES) parameters were recorded for arrhythmia.

Results: Statistically significant differences were observed in the changes in SB, AVB, APB, SVT and VE arrhythmia values in pre-UPPP and post-UPPP periods. Also, in one case the values of arrhythmia in the pre-UPPP period had a positive correlation with the values of the same arrhythmia in the post-UPPP period ($P < 0.001$).

Conclusions: In this study, new information about the effects of UPPP which is one of OSAS treatment methods on cardiac arrhythmias is presented. According to our results, UPPP reduces the rate of SB, AVB, APB, SVT and VES arrhythmias in OSAS patients.

Keywords: Obstructive Sleep Apnea Syndrome, Uvulopalatopharyngoplasty, Cardiac Arrhythmias

1. Background

Obstructive sleep apnea syndrome (OSAS) is shaped by total or partial obstruction of the upper airway during rest like sleeping which results in a decrease in arterial oxygen saturation and transient awakenings (1). OSAS is more common among males who are between 45 - 65 years old and is the most common respiratory disorder related to sleep. Its prevalence in the general adult population ranges from 6% to 17% and can be as high as 49% with advanced age (2). However, this rate is 36% in diabetic sufferers, 63% in sufferers with resistant hypertension, and 71% in sufferers with congestive coronary heart failure and in those with cerebrovascular strokes in acute phase. The sedentary lifestyle has been improving fast in recent years throughout the world along with cigarette and alcohol use, obesity and aging (3-6).

OSAS may present with various symptoms such as chronic fatigue, morning headache, witnessed apnea, ex-

cessive daytime sleepiness or difficulty in concentrating. Also, if OSAS is left untreated, it has some risks such as decreased quality of life, serious medical complications, and increased mortality. Patients with suspected sleep apnea should undergo polysomnography testing (7-9).

Apnea is a temporary stop of breathing for at least 10 seconds during sleep. Hypopnea is a partial obstruction of airflow and is not a temporary stop of breathing. Hypopnea is 30% discount in breath amplitude and 4% discount of oxygen saturation or 50% discount in breath amplitude and 3% reduction of oxygen saturation for more than 10 seconds (10). The variety of apnea-hypopnea episodes in line with hour is known as apnea-hypopnea index (AHI). According to the international clinical sleep disorders-3 (American Academy of Sleep Medicine, AASM); based on AHI and oxygen saturation, severity of OSAS is classified as: (i) mild (AHI is 5 - 15 and oxygen saturation is 85% - 95%); (ii) moderate (AHI is 15 - 30 and oxygen saturation is 65% - 84%);

and (iii) severe (AHI is > 30 and oxygen saturation is $< 64\%$) (10).

The most essential complications of OSAS are connected to the cardiovascular system and OSAS may cause or exacerbate myocardial infarction, congestive heart failure, and atrial fibrillation (11-14). Nocturnal arrhythmias are quite common in OSAS. The most common tachyarrhythmia is early ventricular extrasystole (VES) (15, 16).

Continuous positive airway pressure (CPAP) tool is usually suggested for the OSAS cure (13, 17). Fifty percent of the patients cannot tolerate the CPAP appliance or cannot use it as effective as they should (18). Oral apparatus (such as mandibular advancing device) is recommended as an alternative for patients with mild to moderate OSAS who cannot tolerate CPAP. Patient-specific oral packages are prepared based on patient's characteristics to lessen top airway fall apart and amplify the airway at some stage in sleep (19, 20). Weight loss and positional sleep techniques may be regarded as additional medical measures. Unfortunately, most patients do not benefit from medical treatment.

UPPP was conducted in 1981 by Fujita in order to relieve retropalatal obstruction (anatomical narrowing of the soft palate and uvula) on patients with OSAS (21). In this application, the inferior part of the uvula and soft palate are resected after tonsillectomy. Tonsil plica and the soft palate mucosa in the excised region are mutually sutured. In another study, it was reported that there was a significant regression in cardiovascular system-related complications after UPPP (22). Removing the obstruction in the upper airway is the main principle of surgical treatment of OSAS. Uvulopalatopharyngoplasty (UPPP) is the most common surgical procedure performed by otolaryngologists for the treatment of OSAS (23, 24). In the meta-analysis studies, the success rate for UPPP (with polysomnography) was reported as 50%. However, results from local studies have reported success rates up to 83% (9, 25). In spite of partial reductions in AHI and limited success as a stand-alone treatment option for OSA, UPPP is still an important therapeutic option for many patients who refuse or tolerate CPAP (24). Studies on UPPP and OSAS have extremely focused on its effectiveness and on determining the best patient choice, and there are few data evaluating the effects of UPPP on reducing the incidence of cardiovascular complications in OSAS (14).

2. Objectives

The objective of this study was to investigate possible changes in arrhythmias after UPPP in patients with moderate OSAS who continued having cardiac arrhythmias despite the use of antiarrhythmic drugs and those who could

not tolerate the CPAP device. In addition, we evaluated the correlation between arrhythmias before and after UPPP.

3. Methods

3.1. Patients and Design

This retrospective study included patients from cardiologists and otolaryngologists working as co-authors in this protocol at the Bahat Hospital. The patients who have OSAS and cardiac arrhythmias despite antiarrhythmic treatment (calcium channel blockers and beta blockers) at optimal doses between 2008 - 2017 by the cardiology clinic of the hospital have been included in the study and consulted by the ear, nose, and throat (ENT) clinic.

Patients with OSAS were evaluated with detailed ENT examination, fiberoptic laryngoscopy, Muller maneuver, lateral cephalogram, computed tomography, and magnetic resonance imaging. Finally, 38 patients who did not accept oral apparatus or CPAP treatment were selected and UPPP operation were performed. In addition to arrhythmias, 11 patients had mild hypertension in mild heart diseases and other cardiac diseases were excluded from the study. All patients have undergone UPPP. The operations were performed under general anesthesia (Pentothal 5 mg/kg, Atracurium 0.1 mg/kg, 50% N₂O + 50% O₂ and Isoflurane 1%) after endotracheal intubation. Preoperative and postoperative appearance of oropharynx are shown in Figure 1.

3.2. Arrhythmia Data

The rhythm Holter follow-ups of the patients in the 1st month before UPPP (pre-UPPP) and after UPPP (post-UPPP) in the 6th month were performed by a cardiology center and cardiologists. All patients were followed up with Holter electrocardiography (ELA Spiderview Digital Recorder) during sleep. The recordings were transferred to the computer and evaluated with the Holter program, then visually examined and the parasitic regions were excluded. Sinus bradycardia (SB), atrioventricular block (AVB), atrial premature beat (APB), supraventricular tachycardia (SVT), and ventricular extrasystole (VES) parameters were recorded for arrhythmia.

3.3. Statistical Analyses

Study analysis was carried out with details in SPSS V. 20.00 for Windows package program. The data were recorded mostly as mean \pm standard deviation (SD). In comparison to independent group differences, the student's *t*-test was used when parametric test assumptions were provided, and the Mann Whitney U test was used when not provided.

3.4. Ethical Permission

This study was approved by the Istanbul Yeni Yüzyil University, Non-Interventional Clinical Research Ethics Board (2019/9-02/09/2019). The study was explained in detail to the patients who were included and written informed consent was signed by patients and were obtained from all cases, and the study results were used for scientific aims. The principles of the Declaration of Helsinki and Guidelines for Good Clinical Practices were followed during the study.

4. Results

4.1. Demographic Data

Among patients, 33 (87%) were male and 5 (13%) were female, between 48 and 59 years (the mean age was 54.8 year). All of the patients had moderate OSAS. Endoscopic and imaging examinations have proved that the grade of obstruction was retropalatal in all cases based on the Fujita classification (26).

4.2. Comparison of Arrhythmias

Selected arrhythmia frequency measured before and after UPPP are shown in Table 1. According to these results, statistically significant differences were observed in the changes in SB, AVB, APB, SVT and VE arrhythmia frequency in pre-UPPP and post-UPPP periods ($P < 0.001$).

4.3. Correlations Between Arrhythmias

The correlation results of arrhythmia frequency before and after UPPP are shown in Table 2. According to this table, the frequency of an arrhythmia in the pre-UPPP period had a positive correlation with the values of the same arrhythmia in the post-UPPP period.

In addition, it was determined that *pulse values* did not correlate with any other measurements in both pre-UPPP and post-UPPP periods. *SB value in the pre-UPPP period*: There was a positive and high correlation with pre-UPPP VE and post-UPPP SB values (r values were 0.655 and 0.660, respectively). *AVB value in the pre-UPPP period*: There were a negative and moderate correlation with APB and SVT values in the pre-UPPP period (r values were -0.419 and -0.462, respectively), a positive and strong correlation with post-UPPP AVB values ($r = 0.783$), and a negative and moderate relationship with post-UPPP APB values ($r = 0.418$). *APB in the pre-UPPP period*: There were a positive and very high correlation with pre-UPPP ST values ($r = 0.822$), and positive and high correlations with the APB and ST values in the post-UPPP period (r values were 0.672 and 0.629, respectively). *SVT in the pre-UPPP period*: There were a negative and moderate correlation with post-UPPP AVB ($r = -0.409$), a positive

and high-grade correlation with post-UPPP APB ($r = 0.627$), and a positive and very-high grade relationship with post-UPPP ST ($r = 0.817$). *VES in the pre-UPPP period*: There was a positive and moderate correlation with SB and VES in the post-UPPP period ($r = 0.446$ and $r = 0.567$, respectively). *SB in the post-UPPP period*: there was a positive and weak correlation with post-UPPP APB values ($r = 0.356$). *AVB in the post-UPPP period*: there were a negative and weak relationship with post-UPPP APB ($r = -0.384$) and a negative and moderate relationship with post-UPPP VES values ($r = -0.406$). *APB in the post-UPPP period*: there was a positive and moderate correlation with post-UPPP SVT frequency ($r = 0.521$).

5. Discussion

In this study, we investigated whether arrhythmia changes after UPPP in patients ($n = 38$) with moderate OSAS who have persisting cardiac arrhythmias despite the use of antiarrhythmic drugs and who cannot tolerate CPAP. For this purpose, we evaluated some of the arrhythmia types (SB, AVB, APB, SVT, and VE) in the 1st month before UPPP and in the 6th month after UPPP and recorded their correlations. In this existing study, the implied age of the patients turned into 54.8 years, of which 87% were male. According to our results, statistically significant decreases were observed in all arrhythmia values after UPPP period ($P < 0.001$). In addition, positive and very high correlations were found between APB and SVT values in the pre-UPPP period ($P < 0.001$). There were negative or positive correlations between most of the other parameters except arterial pulse.

By affecting the somatic and autonomic nervous system, OSAS causes adverse effects in the functions of respiratory cardiovascular, gastrointestinal, endocrine, renal and sexual systems. Its most vital aspect outcomes occur inside the cardiovascular system. In OSAS, the most vital reasons of mortality and morbidity are headaches of cardiovascular system (11). Lee et al. evaluated the effects of UPPP on heart disease in a study of 192,316 patients with OSAS (South Korea). They reported that congestive heart failure, atrial fibrillation, and myocardial infarction (in females) were significantly increased in OSAS patients. In addition, UPPP significantly reduced the incidence of congestive heart failure, atrial fibrillation, and myocardial infarction (in some models) in patients with OSAS (14).

In the literature, OSAS has been frequently linked with atrial fibrillation. Beyond atrial fibrillation, OSAS has also been associated with other cardiac rhythm disorders, including sudden cardiac death. Simantirakis and colleagues declared a 22% prevalence of prolonged pauses and bradycardia in moderate-to-severe OSAS patients (27). Patients are assumed to have the “tachy-brady syndrome”

Table 1. Change in Arrhythmia Frequency Before and After Uvulopalatopharyngoplasty (N = 33).

	Pre-UPPP	Post-UPPP	Z	P Value
Pulse	74.42 ± 3.70	74.27 ± 3.88	-0.090	0.929
Sinus bradycardia	4.93 ± 1.43	2.81 ± 1.04	-4.990	< 0.001
Atrioventricular block	1.72 ± 1.03	0.93 ± 0.74	-4.435	< 0.001
Atrial premature beat	5.51 ± 1.46	2.72 ± 1.03	-5.073	< 0.001
Supraventricular tachycardia	3.63 ± 0.99	2.33 ± 0.69	-5.035	< 0.001
Ventricular extrasystole	3.57 ± 0.90	1.54 ± 0.71	-5.088	< 0.001

Abbreviations: Pre-UPPP, before uvulopalatopharyngoplasty operation; Post-UPPP, after uvulopalatopharyngoplasty operation.

Table 2. Correlation of Arrhythmia Frequency Before and After Uvulopalatopharyngoplasty

			Pre-UPPP						Post-UPPP					
			Pulse	SB	AVB	APB	SVT	VES	Pulse	SB	AVB	APB	SVT	VES
Pre-UPPP	Pulse	r	1											
		p												
	SB	r	0.316	1										
		p	0.073											
	AVB	r	-0.010	0.093	1									
		p	0.958	0.605										
	APB	r	0.005	-0.029	-0.419 ^a	1								
		p	0.980	0.871	0.015									
	SVT	r	0.009	-0.082	-0.462 ^b	0.822 ^b	1							
		p	0.959	0.651	0.007	0.000								
	VES	r	0.074	0.655 ^b	-0.194	0.218	0.206	1						
		p	0.682	0.000	0.280	0.222	0.251							
Post-UPPP	Pulse	r	0.005	-0.165	0.019	-0.020	0.091	-0.019	1					
		p	0.979	0.358	0.916	0.912	0.614	0.914						
	SB	r	0.303	0.660 ^b	-0.220	0.207	0.145	0.446 ^b	-0.080	1				
		p	0.087	0.000	0.219	0.248	0.421	0.009	0.659					
	AVB	r	0.066	0.084	0.783 ^b	-0.343	-0.409 ^a	-0.132	-0.048	-0.095	1			
		p	0.715	0.643	0.000	0.051	0.018	0.464	0.791	0.600				
	APB	r	-0.018	0.072	-0.418 ^a	0.672 ^b	0.627 ^b	0.206	0.073	0.356 ^a	-0.384 ^a	1		
		p	0.922	0.689	0.015	0.000	0.000	0.250	0.685	0.042	0.027			
	SVT	r	0.028	-0.168	-0.174	0.629 ^b	0.817 ^b	0.083	0.116	0.043	-0.201	0.521 ^b	1	
		p	0.875	0.351	0.333	0.000	0.000	0.645	0.519	0.811	0.261	0.002		
	VES	r	-0.055	0.340	-0.300	0.202	0.289	0.567 ^b	-0.056	0.264	-0.406 ^a	0.208	0.127	1
		p	0.761	0.053	0.090	0.259	0.102	0.001	0.759	0.138	0.019	0.246	0.481	

Abbreviations: APB, atrial premature beat; AVB, atrioventricular block; Pre-UPPP, before uvulopalatopharyngoplasty operation; Post-UPPP, after uvulopalatopharyngoplasty operation; SB, sinus bradycardia; SVT, supraventricular tachycardia; VES, ventricular extrasystole.

^aCorrelation is significant at the 0.05 level (2-tailed).

^bCorrelation is significant at the 0.01 level (2-tailed).

when such bradyarrhythmias change with atrial fibrillation or other forms of SVT. The ventricular arrhythmias were also reported to be higher among patients with OSAS. Mehra and colleagues showed a significantly higher prevalence of non-sustained ventricular tachycardia (5.3% versus 1.2%, $P = 0.004$) among OSAS patients compared with controls (28). Similarly, severe OSAS was associated with a significantly higher overall risk of complex ventricular ectopy, defined as non-sustained ventricular tachycardia, bigeminy, trigeminy, or quadrigeminy (25% versus 14.5%, $P = 0.002$) (29).

The attacks of hypoxia, increased negative-

intrathoracic pressure and high sympathetic activity are the most common causes of high cardiovascular diseases in patients with OSAS. The intermittent hypoxia due to apnea attacks leads to a decrease in the velocity of cardiac conduction, atrial fibrosis, oxidative stress, and systemic inflammation. In addition, hypoxia induces carotid chemoreceptors and leads to catecholamine discharge and vasoconstriction. Pulmonary vasoconstriction and pulmonary hypertension may also occur due to alveolar hypoxia. Recurrent hypoxia attacks during sleep cause acute elevations in pulmonary artery pressure (30, 31).

Increased negative intrathoracic pressure secondary

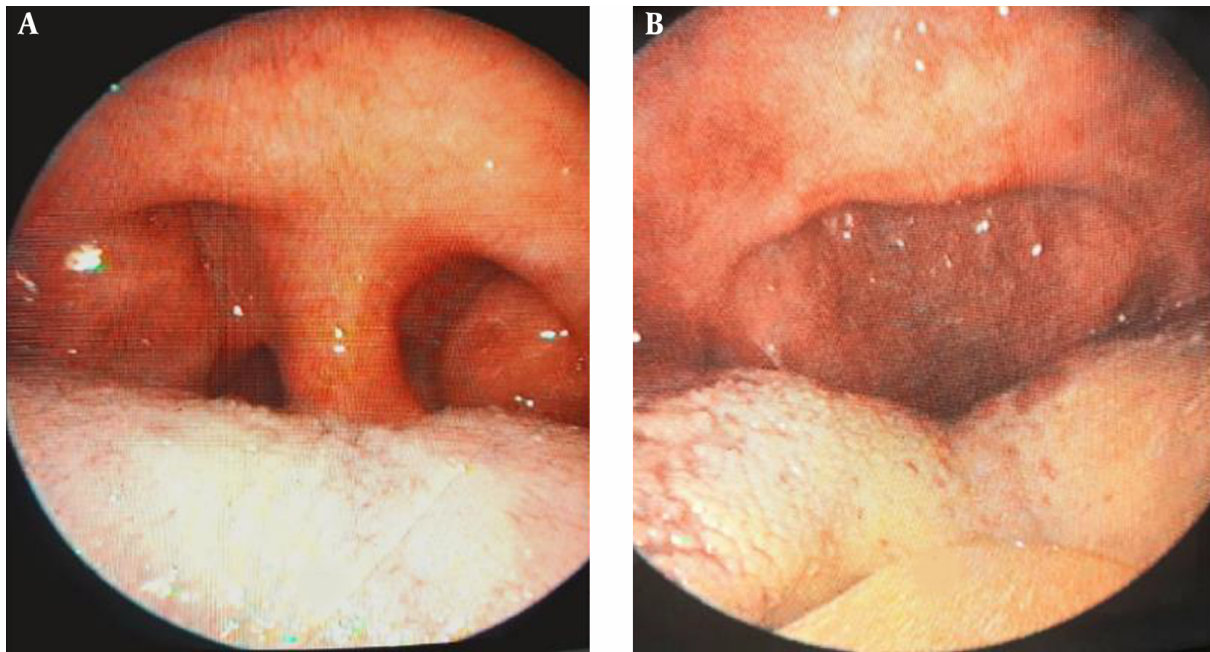


Figure 1. Appearance of oropharynx: A, pre-Uvulopalatopharyngoplasty (UPPP), B, post-UPPP

to increased inspiratory effort due to airway obstruction increases the afterload of heart and leads to left ventricle and left atrial hypertrophy, hypertension, and cardiac arrhythmias (8, 32). Negative intrathoracic pressure fluctuations throughout obstructive attacks increase catecholamine release and so on increase atrial and intrathoracic aortic wall stress, as a result it also increases the likelihood of nocturnal atrial arrhythmias and thoracic aortic dissection (33).

High sympathetic activity due to awakening and fear of death at the end of apnea reduces heart rate variability and increases blood pressure. The three main points mentioned above, and other sequelae probably contribute to an increased risk of cardiac arrhythmias, congestive heart failure and myocardial infarction in OSAS patients (12, 14, 34). Another factor causing catecholamine discharges is the “stimulation” response that pauses the apnea. Another study reported that catecholamine levels in the blood and urine of patients with OSAS decreased slowly after CPAP treatment (35).

In our study, the types of correlations (positive and negative) between arrhythmias in the 1st month before and the 6th month after UPPP are shown in Table 3. According to this table, the frequency of an arrhythmia in the pre-UPPP period has a positive correlation with the values of the same arrhythmia in the post-UPPP period. The values of pre-UPPP APB were positively correlated with three param-

eters (pre-UPPP SVT, post-UPPP APB, and post-UPPP SVT). It is known that supraventricular arrhythmias have correlations among themselves and ventricular arrhythmias have correlations among themselves too (9, 14, 29). Positive correlations between APB and SVT in pre- and post-UPPP periods can also be explained in this relationship. In addition, there were negative correlations between pre-UPPP AVB and three parameters (pre-UPPP APB, pre-UPPP SVT, and post-UPPP APB).

SB value in the pre-UPPP period: there was a positive and high correlation with pre-UPPP VE and post-UPPP SB values (r values were 0.655 and 0.660, respectively). *AVB value in the pre-UPPP period:* there were a negative and moderate correlation with APB and SVT values in the pre-UPPP period (r values were -0.419 and -0.462, respectively), a positive and strong correlation with post-UPPP AVB values ($r = 0.783$), and a negative and moderate relationship with post-UPPP APB values ($r = 0.418$). *APB in the pre-UPPP period:* there were positive and very high correlation with pre-UPPP ST values ($r = 0.822$), and positive and high correlations with the APB and ST values in the post-UPPP period (r values were 0.672 and 0.629, respectively). *SVT in the pre-UPPP period:* there were a negative and moderate correlation with post-UPPP AVB ($r = -0.409$), a positive and high-grade correlation with post-UPPP APB ($r = 0.627$), and a positive and very-high grade relationship with post-UPPP ST ($r = 0.817$). *VES in the pre-UPPP period:* there were a positive and moderate correlation with

Table 3. The Correlation Types of Arrhythmias Before and After Uvulopalatopharyngoplasty

Correlations		
Positive Correlations		
Pre-UPPP SB	And	pre-UPPP VES ve post-UPPP SB
Pre-UPPP AVB		post-UPPP AVB
Pre-UPPP APB		pre-UPPP SVT, post-UPPP APB ve post-UPPP SVT
Pre-UPPP SVT		post-UPPP APB ve post-UPPP SVT
Pre-UPPP VES		post-UPPP SB ve post-UPPP VES
Post-UPPP SB		post-UPPP APB
Negative Correlations		
Pre-UPPP AVB	And	pre-UPPP APB, pre-UPPP SVT ve post-UPPP APB
Pre-UPPP SVT		post-UPPP AVB
Pre-UPPP APB		post-UPPP APB ve post-UPPP VES

Abbreviations: APB, atrial premature beat; AVB, atrioventricular block; Pre-UPPP, before uvulopalatopharyngoplasty operation; Post-UPPP, after uvulopalatopharyngoplasty operation; SB, sinus bradycardia; SVT, supraventricular tachycardia; VES, ventricular extrasystole.

SB and VES in the post-UPPP period ($r = 0.446$ and $r = 0.567$, respectively). *SB in the post-UPPP period*: there was a positive and weak correlation with post-UPPP APB values ($r = 0.356$). *AVB in the post-UPPP period*: there were a negative and weak relationship with post-UPPP APB ($r = -0.384$) and a negative and moderate relationship with post-UPPP VES values ($r = -0.406$). *APB in the post-UPPP period*: there was a positive and moderate correlation with post-UPPP SVT values ($r = 0.521$).

5.1. Limitations of the Study

However, there are several obstacles to this work that should be acknowledged. First of all, for easier design, faster completion and more understandable interpretation of our study, we did not evaluate OSAS patients' concomitant diseases such as hypertension, DM, BMI, and dyslipidemia and we did not record their changes after UPPP. However, the relationships between these diseases and both OSAS and arrhythmias should be considered, and these parameters should be considered in regression and correlation analyses.

Secondly, we assessed the effect of UPPP on arrhythmias in just as short as six months, because this time was enough for us to confirm our hypothesis. Also, researches on the long-term effects of UPPP have been harsh in terms of compliance and cost of patients. For this reason and for the reasons stated in the first limitation, we did not evaluate long-term arrhythmia outcomes such as 1, 2 and 3 years after UPPP. However, it is known that the recovery periods of some chronic diseases may take a long time. Therefore, particularly in regression and correlation analyses, time-

dependent changes of some positive and negative relationships should be considered for the researchers.

In addition, the lack of assessment of the AHI after UPPP and the evaluation of arrhythmias only in moderate OSAS patients are other limitations of our study.

5.2. Conclusions

In this study, new information about the effects of UPPP which is one of OSAS treatment methods on cardiac arrhythmias is presented. According to our results, UPPP reduces the rate of SB, AVB, APB, SVT and VES arrhythmias in OSAS patients.

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Footnotes

Authors' Contribution: All studies except cardiology were done by Ali Seyed Resuli.

Conflict of Interests: The authors announced that they have no conflict of interest in regard to this investigation.

Ethical Approval: This study was approved by the İstanbul Yeni Yüzyıl University, Non-Interventional Clinical Research Ethics Board (2019/9-02/09/2019).

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References

- Nam H, Lim JS, Kim JS, Lee KJ, Koo DL, Lee C. Sleep Perception in Obstructive Sleep Apnea: A Study Using Polysomnography and the Multiple Sleep Latency Test. *J Clin Neurol*. 2016;**12**(2):230-5. doi: [10.3988/jcn.2016.12.2.230](https://doi.org/10.3988/jcn.2016.12.2.230). [PubMed: [27074296](https://pubmed.ncbi.nlm.nih.gov/27074296/)]. [PubMed Central: [PMC4828571](https://pubmed.ncbi.nlm.nih.gov/PMC4828571/)].
- Senaratna CV, Perret JL, Lodge CJ, Lowe AJ, Campbell BE, Matheson MC, et al. Prevalence of obstructive sleep apnea in the general population: A systematic review. *Sleep Med Rev*. 2017;**34**:70-81. doi: [10.1016/j.smrv.2016.07.002](https://doi.org/10.1016/j.smrv.2016.07.002). [PubMed: [27568340](https://pubmed.ncbi.nlm.nih.gov/27568340/)].
- Elmasry A, Lindberg E, Berne C, Janson C, Gislason T, Awad Tageldin M, et al. Sleep-disordered breathing and glucose metabolism in hypertensive men: a population-based study. *J Intern Med*. 2001;**249**(2):153-61. doi: [10.1046/j.1365-2796.2001.00787.x](https://doi.org/10.1046/j.1365-2796.2001.00787.x). [PubMed: [11240844](https://pubmed.ncbi.nlm.nih.gov/11240844/)].
- Logan AG, Perlikowski SM, Mente A, Tisler A, Tkacova R, Niroumand M, et al. High prevalence of unrecognized sleep apnoea in drug-resistant hypertension. *J Hypertens*. 2001;**19**(12):2271-7. doi: [10.1097/00004872-200112000-00022](https://doi.org/10.1097/00004872-200112000-00022). [PubMed: [11725173](https://pubmed.ncbi.nlm.nih.gov/11725173/)].
- Parra O, Arboix A, Bechich S, Garcia-Eroles L, Montserrat JM, Lopez JA, et al. Time course of sleep-related breathing disorders in first-ever stroke or transient ischemic attack. *Am J Respir Crit Care Med*. 2000;**161**(2 Pt 1):375-80. doi: [10.1164/ajrccm.161.2.9903139](https://doi.org/10.1164/ajrccm.161.2.9903139). [PubMed: [10673174](https://pubmed.ncbi.nlm.nih.gov/10673174/)].

6. Sin DD, Fitzgerald F, Parker JD, Newton G, Floras JS, Bradley TD. Risk factors for central and obstructive sleep apnea in 450 men and women with congestive heart failure. *Am J Respir Crit Care Med*. 1999;**160**(4):1101–6. doi: [10.1164/ajrccm.160.4.9903020](#). [PubMed: [10508793](#)].
7. Malhotra A, White DP. Obstructive sleep apnoea. *The Lancet*. 2002;**360**(9328):237–45. doi: [10.1016/S0140-6736\(02\)09464-3](#).
8. Porto F, Sakamoto YS, Salles C. Association between Obstructive Sleep Apnea and Myocardial Infarction: A Systematic Review. *Arq Bras Cardiol*. 2017;**108**(4):361–9. doi: [10.5935/abc.20170031](#). [PubMed: [28380133](#)]. [PubMed Central: [PMC5421476](#)].
9. Tietjens JR, Claman D, Kezirian EJ, De Marco T, Mirzayan A, Sadroonri B, et al. Obstructive Sleep Apnea in Cardiovascular Disease: A Review of the Literature and Proposed Multidisciplinary Clinical Management Strategy. *J Am Heart Assoc*. 2019;**8**(1). e010440. doi: [10.1161/JAHA.118.010440](#). [PubMed: [30590966](#)]. [PubMed Central: [PMC6405725](#)].
10. Sateia MJ. International classification of sleep disorders-third edition: highlights and modifications. *Chest*. 2014;**146**(5):1387–94. doi: [10.1378/chest.14-0970](#). [PubMed: [25367475](#)].
11. Seyed Resuli A. Cardiovascular Complications in Obstructive Sleep Apnea Syndrome. *Multidisciplinary Cardiovascular Annals*. 2019;**11** Press(In Press). doi: [10.5812/mca.91534](#).
12. Goudis CA, Ketikoglou DG. Obstructive sleep and atrial fibrillation: Pathophysiological mechanisms and therapeutic implications. *Int J Cardiol*. 2017;**230**:293–300. doi: [10.1016/j.ijcard.2016.12.120](#). [PubMed: [28040290](#)].
13. Garcia-Rio F, Alonso-Fernandez A, Armada E, Mediano O, Lores V, Rojo B, et al. CPAP effect on recurrent episodes in patients with sleep apnea and myocardial infarction. *Int J Cardiol*. 2013;**168**(2):1328–35. doi: [10.1016/j.ijcard.2012.12.015](#). [PubMed: [23302113](#)].
14. Lee HM, Kim HY, Suh JD, Han KD, Kim JK, Lim YC, et al. Uvulopalatopharyngoplasty reduces the incidence of cardiovascular complications caused by obstructive sleep apnea: results from the national insurance service survey 2007–2014. *Sleep Med*. 2018;**45**:11–6. doi: [10.1016/j.sleep.2017.12.019](#). [PubMed: [29680418](#)].
15. Guilleminault C, Connolly SJ, Winkle RA. Cardiac arrhythmia and conduction disturbances during sleep in 400 patients with sleep apnea syndrome. *The American Journal of Cardiology*. 1983;**52**(5):490–4. doi: [10.1016/0002-9149\(83\)90013-9](#).
16. Hohl M, Linz B, Böhm M, Linz D. Obstructive sleep apnea and atrial arrhythmogenesis. *Curr Cardiol Rev*. 2014;**10**(4):362–8. doi: [10.2174/1573403X1004140707125137](#). [PubMed: [25004989](#)]. [PubMed Central: [PMC4101201](#)].
17. Abuzaid AS, Al Ashry HS, Elbadawi A, Ld H, Saad M, Elgendy IY, et al. Meta-Analysis of Cardiovascular Outcomes With Continuous Positive Airway Pressure Therapy in Patients With Obstructive Sleep Apnea. *Am J Cardiol*. 2017;**120**(4):693–9. doi: [10.1016/j.amjcard.2017.05.042](#). [PubMed: [28651851](#)].
18. Weaver TE, Grunstein RR. Adherence to continuous positive airway pressure therapy: the challenge to effective treatment. *Proc Am Thorac Soc*. 2008;**5**(2):173–8. doi: [10.1513/pats.200708-119MG](#). [PubMed: [18250209](#)]. [PubMed Central: [PMC2645251](#)].
19. Epstein LJ, Kristo D, Strollo PJ Jr, Friedman N, Malhotra A, Patil SP, et al. Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. *J Clin Sleep Med*. 2009;**5**(3):263–76. [PubMed: [19960649](#)]. [PubMed Central: [PMC2699173](#)].
20. Kushida CA, Littner MR, Morgenthaler T, Alessi CA, Bailey D, Coleman J Jr, et al. Practice parameters for the indications for polysomnography and related procedures: an update for 2005. *Sleep*. 2005;**28**(4):499–521. doi: [10.1093/sleep/28.4.499](#). [PubMed: [16171294](#)].
21. Fujita S, Conway W, Zorick F, Roth T. Surgical correction of anatomic abnormalities in obstructive sleep apnea syndrome: uvulopalatopharyngoplasty. *Otolaryngol Head Neck Surg*. 1981;**89**(6):923–34. doi: [10.1177/019459988108900609](#). [PubMed: [6801592](#)].
22. Baradaranfar MH, Edalatkhah M, Dadgarnia MH, Atighechi S, Behniafard N, Mirvakili A, et al. The effect of uvulopalatopharyngoplasty with tonsillectomy in patients with obstructive sleep apnea. *Indian J Otolaryngol Head Neck Surg*. 2015;**67**(Suppl 1):29–33. doi: [10.1007/s12070-014-0735-1](#). [PubMed: [25621250](#)]. [PubMed Central: [PMC4298602](#)].
23. Aurora RN, Casey KR, Kristo D, Auerbach S, Bista SR, Chowdhuri S, et al. Practice parameters for the surgical modifications of the upper airway for obstructive sleep apnea in adults. *Sleep*. 2010;**33**(10):1408–13. doi: [10.1093/sleep/33.10.1408](#). [PubMed: [21061864](#)]. [PubMed Central: [PMC2941428](#)].
24. Choi JH, Cho SH, Kim SN, Suh JD, Cho JH. Predicting Outcomes after Uvulopalatopharyngoplasty for Adult Obstructive Sleep Apnea: A Meta-analysis. *Otolaryngol Head Neck Surg*. 2016;**155**(6):904–13. doi: [10.1177/0194599816661481](#). [PubMed: [27484230](#)].
25. Stuck BA, Ravesloot MJL, Eschenhagen T, de Vet HCW, Sommer JU. Uvulopalatopharyngoplasty with or without tonsillectomy in the treatment of adult obstructive sleep apnea - A systematic review. *Sleep Med*. 2018;**50**:152–65. doi: [10.1016/j.sleep.2018.05.004](#). [PubMed: [30056286](#)].
26. Fujita S; Guilleminault C. Surgical treatment of obstructive sleep apnea. UPPP and lingualplasty (laser midline glossectomy). *Obstructive sleep apnea syndrome: Clinical research and treatment*. New York: Raven Press; 1990. p. 129–51.
27. Simantirakis EN, Schiza SI, Marketou ME, Chrysostomakis SI, Chlouverakis GI, Klapsinos NC, et al. Severe bradyarrhythmias in patients with sleep apnoea: the effect of continuous positive airway pressure treatment: a long-term evaluation using an insertable loop recorder. *Eur Heart J*. 2004;**25**(12):1070–6. doi: [10.1016/j.ehj.2004.04.017](#). [PubMed: [15191779](#)].
28. Mehra R, Benjamin EJ, Shahar E, Gottlieb DJ, Nawab R, Kirchner HL, et al. Association of nocturnal arrhythmias with sleep-disordered breathing: The Sleep Heart Health Study. *Am J Respir Crit Care Med*. 2006;**173**(8):910–6. doi: [10.1164/rccm.200509-1442OC](#). [PubMed: [16424443](#)]. [PubMed Central: [PMC2662909](#)].
29. Patel N, Donahue C, Shenoy A, Patel A, El-Sherif N. Obstructive sleep apnea and arrhythmia: A systemic review. *Int J Cardiol*. 2017;**228**:967–70. doi: [10.1016/j.ijcard.2016.11.137](#). [PubMed: [27914359](#)].
30. Shepard JW. Cardiopulmonary Consequences of Obstructive Sleep Apnea. *Mayo Clinic Proceedings*. 1990;**65**(9):1250–9. doi: [10.1016/S0025-6196\(12\)62749-9](#).
31. Laks L, Lehrhaft B, Grunstein RR, Sullivan CE. Pulmonary artery pressure response to hypoxia in sleep apnea. *Am J Respir Crit Care Med*. 1997;**155**(1):193–8. doi: [10.1164/ajrccm.155.1.9001311](#). [PubMed: [9001311](#)].
32. Lyons OD, Bradley TD. Heart Failure and Sleep Apnea. *Can J Cardiol*. 2015;**31**(7):898–908. doi: [10.1016/j.cjca.2015.04.017](#). [PubMed: [26112300](#)].
33. Kasai T, Floras JS, Bradley TD. Sleep apnea and cardiovascular disease: a bidirectional relationship. *Circulation*. 2012;**126**(12):1495–510. doi: [10.1161/CIRCULATIONAHA.111.070813](#). [PubMed: [22988046](#)].
34. Eckert DJ, Malhotra A. Pathophysiology of adult obstructive sleep apnea. *Proc Am Thorac Soc*. 2008;**5**(2):144–53. doi: [10.1513/pats.200707-114MG](#). [PubMed: [18250206](#)]. [PubMed Central: [PMC2628457](#)].
35. Fletcher EC. Sympathetic activity and blood pressure in the sleep apnea syndrome. *Respiration*. 1997;**64** Suppl 1:22–8. doi: [10.1159/000196732](#). [PubMed: [9380957](#)].